

## REMARKS

Claims 1-18 are pending in the application. Claims 4, 5, and 11-18 are under examination. Claims 1-3 and 6-10 are withdrawn in response to the prior restriction requirement. In the Office Action mailed August 19, 2008, claim 4 is objected to because of an informality. Claims 12, 13, 15, and 16 are rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. Claims 4-5, and 11-18 are rejected under 35 U.S.C. 112, second paragraph as being indefinite. Claims 4 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Pat. App. Pub. No. 2003/0171325 (Gascoyne et al., hereinafter "Gascoyne").

### **I. Claim Objections**

Claim 4 is objected to because of an informality, the recitation of "nucleic acid" in step b) instead of "a nucleic acid" or "nucleic acids". The Applicants have herein amended claim 4 to adopt the Examiner's recommendation by replacing "nucleic acid" with "a nucleic acid". No new matter is added by this amendment. Entry of this amendment and withdrawal of the objection to claim 4 is therefore respectfully requested.

### **II. Rejections under 35 U.S.C. 112, first paragraph**

Claims 12, 13, 15, and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for allegedly containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, claims 12 and 15 are rejected because the passages of the specification suggested by the Applicants allegedly fail to define or provide any disclosure to support the claim limitation "detecting a change in electrophoretic force exerted by the synthesized nucleic acid on the solid support as it grows." The Office Action particularly states in response to the Applicants' arguments submitted May 19, 2008 that "paragraphs [0022] and [0119] of US 2005/0227235A1 (the published application) do not describe 'detecting change in electrophoretic force exerted by the synthesized nucleic acid on the support as it grows' as recited in claims 12 and 15 because claims 12 and 15 do not limit the support as a particle or bead" [August 19, 2008 Office Action at page 5, continuation of item 4].

The Applicants respectfully traverse the rejections of claims 12 and 15. In order to clarify that the electrophoretic force created by the growing nucleic acid is exerted on a support that is a bead or particle, the Applicants have herein amended claims 12 and 15 to adopt the Examiner's suggestion and recite that the solid support is a bead or particle. Support for these amendments is found in the published application (US2005/0227235A1) at least at paragraphs [0022], [0118]-[0120], and [0137]-[0143], and in Figs. 9A and 9B. No new matter is added by these amendments, entry of which is respectfully requested. The Applicants therefore respectfully maintain that this limitation of claims 12 and 15, as amended, is fully supported by the written description, that it is clear that the inventors, at the time the application was filed, had possession of the claimed invention, that the underlying technology of the limitation is well-known in the art of the invention, and that the rejected claims therefore satisfy the requirements of 35 U.S.C. 112, first paragraph. Reconsideration and withdrawal of the rejections of claims 12 and 15, as amended, under 35 U.S.C. 112, first paragraph, is therefore respectfully requested.

Claims 13 and 16 are rejected in particular because the passages of the specification, Figures, and originally filed claim 7 cited by the Applicants allegedly "do not describe a limitation 'a plurality of reactions comprising steps (a)-(e) are carried out in parallel using a plurality of light sources and detectors'". The Office Action indicates that "paragraphs [0026], [0027] and [0125]-[0130] of the specification, Figures 11A, 11B, 12A and 12B, and original claim 7 suggested by applicant describe that parallel single-molecule systems may use arrays of light sources and detectors and describe the parallelization of single-molecule systems with and without arrays of light sources and detectors" but that the cited sections do not describe the cited limitation [August 19, 2008 Office Action at page 3, continuation of item 4].

The Applicants respectfully traverse the rejections of claims 13 and 16. In order to clarify that the single-molecule system of the claimed invention may use arrays of light sources and detectors, whether alone or when several such systems are used in parallel, the Applicants have herein amended claims 13 and 16 to adopt the Examiner's suggestion and recite that the steps of the claimed independent methods are carried out using a plurality of light sources and detectors. Support for these amendments is found in the published application (US2005/0227235A1) at least at paragraphs [0026] and [0125] of the published application, Fig. 11A, and original claim 7. No new matter is added by these amendments, entry of which is respectfully requested. The Applicants therefore respectfully maintain that this limitation of claims 13 and 16, as amended, is fully supported by the written description, that it is clear that

the inventors, at the time the application was filed, had possession of the claimed invention, that the underlying technology of the limitation is well-known in the art of the invention, and that the rejected claims therefore satisfy the requirements of 35 U.S.C. 112, first paragraph.

Reconsideration and withdrawal of the rejections of claims 13 and 16, as amended, under 35 U.S.C. 112, first paragraph, is therefore respectfully requested.

### **III. Rejections under 35 U.S.C. 112, second paragraph**

Claims 4, 5, and 11-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. As a preliminary matter, the Applicants note that, while claims 13, 16, and 17 are stated as being rejected under this section, no explanation of the reason for rejection of these claims is given. Because it is unclear why claims 13, 16, and 17 have been rejected under this section, no response to the rejection of them can be made. Clarification of the reasons for rejection of claims 13, 16, and 17 under this section, or withdrawal of the rejections, is therefore respectfully requested.

Claim 4 is rejected as being vague and indefinite because “it is unclear whether ‘errors’ in step d) is identical to errors in step e)”. The Applicants have herein amended claim 4 to adopt the Examiner’s recommendation by replacing “errors” in step e) with “the errors”. No new matter is added by this amendment. Entry of this amendment and withdrawal of the rejection of claim 4, as amended, under 35 U.S.C. 112, second paragraph, is therefore respectfully requested.

Claim 11 is rejected as being vague and indefinite because “[s]ince the claim does not indicate that the composition of a deprotection wash, it is unclear why the deprotection wash can deprotect the synthesized nucleic acid.” In light of the amendments to claim 5 discussed below, the Applicants have herein cancelled claim 11, rendering this rejection moot.

Claim 18 is rejected as being vague and indefinite because “[s]ince claim 5 only describes deletion errors”, “claims 5 and 18 do not correspond [to] each other.” The Applicants have herein cancelled claim 18, rendering this rejection moot.

Claims 12 and 15 are rejected as being vague and indefinite because “[s]ince the claim does not indicate how electrophoretic force is correlated with [the] synthesized growing nucleic acid on the solid support as it grows, it is unclear why change in electrophoretic force can be exerted by the synthesized growing nucleic acid on the solid support as it grows.” The Applicants respectfully traverse the rejections of claims 12 and 15. In order to clarify why a change in electrophoretic force is exerted by the synthesized nucleic acid as it grows, the

Applicants have herein amended claims 12 and 15 to recite that the step of detecting detects an increase in electrophoretic force exerted by the synthesized nucleic acid on the solid support, the increase in electrophoretic force being caused by the growth of the synthesized nucleic acid.

Support for these amendments is found in the published application (US2005/0227235A1) at least at paragraphs [0022], [0118]-[0120], and [0137]-[0143], and in Figs. 9A, 9B, and 15A-E. No new matter is added by these amendments. Entry of these amendments and reconsideration and withdrawal of the rejections of claims 12 and 15, as amended, under 35 U.S.C. 112, second paragraph, is therefore respectfully requested.

Claim 5 is rejected as being vague and indefinite because “[s]ince the claim does not indicate that the sequence of the synthesized nucleic acid has deletion errors in the sequence and how the deletion errors in the sequence of the synthesized nucleic acid is correlated with the deprotection of the 5’ protecting group, it is unclear why deletion errors in the sequence of the synthesized nucleic acid can be eliminated by the step of monitoring the deprotection of the 5’ protecting group as recited in step b)”. Claim 14 is rejected similarly, with the additional reason that “claim 4 does not indicate that the sequence of the synthesized nucleic acid has at least one 5’ protecting group.”

The Applicants respectfully traverse the rejections of claims 5 and 14. In order to clarify that the sequence of the synthesized nucleic acid has deletion errors and the mechanism by which deletion errors in the sequence of the synthesized nucleic acid can be eliminated by the step of monitoring deprotection of the 5’ protecting group, the Applicants have herein amended claims 5 and 14 to recite that the step of eliminating eliminates any deletion errors present in the sequence of the synthesized nucleic acid, by the steps of deprotecting the synthesized nucleic acid by using a deprotection wash to remove at least one 5’ protecting group, flowing the deprotection wash and any removed 5’ protecting group through a channel opening, monitoring the flowed wash for the presence or absence of a removed 5’ protecting group, and recycling the flowed wash until the presence of at least one 5’ protecting group is detected in the wash. In addition, the Applicants have herein also amended claim 14 to recite that the synthesized nucleic acid has at least one 5’ protecting group. Support for these amendments is found in the published application (US2005/0227235A1) at least at paragraphs [0029]-[0030] and [0136], and in Fig. 14B. No new matter is added by these amendments. Entry of these amendments and reconsideration and withdrawal of the rejections of claims 5 and 14, as amended, under 35 U.S.C. 112, second paragraph, is therefore respectfully requested.

#### **IV. Rejections under 35 U.S.C. 102(e)**

Claims 4 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Gascoyne. The Applicants respectfully traverse the rejections. Gascoyne does not teach the claimed invention of the Applicants, as Gascoyne fails to teach the Applicants' claimed element of passing the solid support and the synthesized nucleic acid through a channel opening.

In the Applicants' claimed invention, a nucleic acid is synthesized attached to a solid support such as a bead or particle. In order to detect errors during synthesis, the synthesized nucleic acid, together with the support, are subjected to a detection step during which they are passed together through the opening of a channel, also called a nanopore [published application at paragraphs [0029] and [0135], and Fig. 14A]. In contrast, Gascoyne merely teaches synthesis of a nucleic acid attached to a bead within a microfluidic device that happens to have one or more channels. In particular, in the passages and figure (Fig. 1) cited by the Office Action [August 19, 2008 Office Action at page 8, item 14], it is clear that the "top right of the center channel" cited by the Office Action is merely the channel by which new beads are injected into the system from the bead reservoir, that the synthesis of nucleic acids on the bead support takes place solely within the center chamber of the device, and that the synthesized nucleic acid and dielectric beads never pass together through any channel within the device, but rather are trapped and collected by the "accumulator and trapping electrode" pictured in the center of Fig. 1 [Gascoyne at Fig. 1 and paragraphs [0038]-[0039]]. Gascoyne therefore fails to teach passing the solid support and the synthesized nucleic acid through a channel opening, as is recited in the Applicants' claim 4. This deficiency of Gascoyne is not cured by any other art of record, none of which teaches passing the solid support and the synthesized nucleic acid through a channel opening, in combination with the other claimed elements of the Applicants invention, as recited in independent claim 4 of the Applicants. As Gascoyne fails to teach all the elements of the Applicants' claim 4, Gascoyne fails to anticipate or make obvious the Applicants' claimed invention. Reconsideration and withdrawal of the rejections of claim 4 over Gascoyne is therefore respectfully requested.

Furthermore, in order to clarify and to more distinctly claim and point out that, in the Applicants' invention, the step of passing through the channel opening is directly related to the step of detecting errors in the sequence of the synthesized nucleic acid, the Applicants have herein amended independent claim 4 to recite that the channel opening supports at least one

detector and that the step of detecting uses the at least one detector located at the channel opening. Support for this amendment is found in the published application (US2005/0227235A1) at least at paragraphs paragraphs [0029] and [0135], and in Fig. 14A. No new matter is added by this amendment, entry of which is therefore respectfully requested. Passing the combined synthesized nucleic acid and solid support through a channel opening supporting at least one detector in order to detect errors in the synthesized nucleic acid is not taught by Gascoyne. This deficiency of Gascoyne is not cured by any other art of record, none of which teach passing the combined synthesized nucleic acid and solid support through a channel opening supporting at least one detector in order to detect errors in the synthesized nucleic acid in combination with the other claimed elements of the Applicants invention, as recited in currently amended independent claim 4 of the Applicants. Gascoyne therefore fails to anticipate or make obvious the Applicants' invention, whether taken alone or in combination with any other art of record. Reconsideration and withdrawal of the rejections of claim 4, as amended, over Gascoyne is therefore respectfully requested.

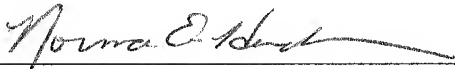
Claim 17 depends from currently amended claim 4, which is not anticipated or made obvious by Gascoyne, as discussed above, because Gascoyne fails to teach passing the solid support and the synthesized nucleic acid through a channel opening supporting at least one detector in order to detect errors in the synthesized nucleic acid. These deficiencies of Gascoyne are not cured by any other art of record. As a dependent claim, claim 17 also requires passing the solid support and the synthesized nucleic acid through a channel opening supporting at least one detector in order to detect errors in the synthesized nucleic acid, so claim 17 is therefore not anticipated or made obvious by Gascoyne. Reconsideration and withdrawal of the rejection of claim 17 is therefore respectfully requested. Furthermore, because claim 17 depends from currently amended independent claim 4, which is in condition for allowance, claim 17 is also in condition for allowance. Reconsideration and withdrawal of the rejection of claim 17 is therefore also respectfully requested.

## **V. Conclusion**

Claims 11 and 18 have been cancelled. Claims 4, 5, and 12-16 have been amended. No new matter is presented by these amendments. The Applicants respectfully submit that claims 4, 5, and 12-17 are now in condition for allowance, which action is now requested. For this reason, and in view of the foregoing arguments, the Applicants believe that this application is now in

condition for allowance, which action is respectfully solicited. Should there remain any unresolved issues, it is respectfully requested that the Examiner telephone Norma E. Henderson, Applicants' Attorney, at 603-437-4400, so that such issues may be resolved as expeditiously as possible.

Respectfully Submitted,



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